DESIGN OF BETA-SHEET PROTEINS WITH SPECIFIC BINDING PROPERTIES

What is claimed is:

~~AMENDED CLAIMS~~

Sub A1

1. Protein with beta-sheet structure,
characterized in that
amino acids exposed on the surface in at least two β-strands exposed on the surface of at least one beta sheet exposed on the surface are specifically substituted, deleted or inserted, such that the protein has new specific antigen binding properties or a new catalytic activity or new fluorescence properties.

2. Protein according to Claim 1,
characterized in that
it is included in the group consisting of crystallines, spherulines, heat shock proteins, cold shock proteins, β-helix proteins, lipocalins, serpins, fibronectins or transcription factors or is GFP, NGF, tendamistat or lysozyme.

3. Protein according to Claim 1 or 2,
characterized in that,
amino acids exposed on the surface in three beta strands exposed on the surface are substituted, deleted or inserted.

4. Protein according to Claim 1 or 2,
characterized in that,
amino acids exposed on the surface in four or more beta strands exposed on

the surface are substituted, deleted or inserted.

5. Protein according one or more of the preceding claims,
characterized in that
amino acids exposed on the surface in at least two beta strands in at least two beta sheets are substituted, deleted or inserted.

Sub A1 Cont.

6. Protein according to one or more of the preceding claims,
characterized in that,
amino acids exposed on the surface in three beta strands in two antiparallel beta sheets are substituted, deleted or inserted.

7. Protein according to one or more of the preceding claims,
characterized in that
it is a crystalline of vertebrates, preferably rodents, birds or fish.

8. Protein according to one or more of the preceding claims,
characterized in that,
it is an alpha-, beta- or gamma-crystalline.

9. Protein according to one or more of the preceding claims,
characterized in that,
it is a gamma-II-crystalline protein.

10. Protein according to one or more of the preceding claims,
characterized in that
amino acids exposed on the surface of the protein are substituted, deleted or inserted in a region of the beta sheet accessible to a solvent or to a binding partner.

11. Protein according to one or more of the preceding claims,
characterized in that,
amino acids exposed on the surface are substituted, deleted or inserted in a β-sheet structure of a domain or a subunit of the protein.

12. Protein according to one or more of the preceding claims, characterized in that, it is a gamma-II-crystalline which has been obtained by substitution, deletion or insertion of one or more of the amino acids Lys 2, Thr 4, Tyr 6, Cys 15, Glu 17, Ser 19, Arg 36 and Asp 38 in gamma-II-crystalline.

13. Protein according to one or more of the preceding claims, characterized in that, amino acids exposed on the surface of the protein have been substituted, deleted or inserted in the beta sheet such that it has antibody-like binding properties or an enzymic (catalytic) activity.

14. Protein according to Claim 12 or 13, characterized in that it has binding specificity for estradiol or the conjugate thereof, BSA-β-estradiol-17-hemisuccinate.

15. Protein according to one or more of the preceding claims, characterized in that, it has binding specificity for estradiol or the conjugate thereof, BSA-β-estradiol-17-hemisuccinate and has the amino acid sequence SEQ ID NO. 19 or SEQ ID NO. 21.

16. Protein according to one or more of the preceding claims, characterized in that, it is combined with other proteins or non-protein substances.

17. DNA coding for a protein according to one or more of the preceding claims.

18. RNA derived from the DNA according to Claim 17.

19. Prokaryotic or eukaryotic vectors or cells comprising a DNA or RNA according to Claim 17 or 18 or parts thereof coding for functional regions of the protein.

20. Method for preparing a protein according to one or more of the preceding claims, comprising the following steps:

sub f/2 Cont.

a. Mutagenesis of the DNA coding for a protein with beta-sheet structure in those regions which code for at least two beta strands, exposed on the surface, of a beta sheet exposed on the surface;

b. Expression of the mutants obtained in step (a) in a suitable expression system; and

c. Selection and isolation of mutants having the desired binding properties and/or the desired catalytic activity; optionally

d. Expression and purification of the beta sheet-mutated proteins.

21. Method according to Claim 20, characterized in that the mutagenesis comprises a substitution, deletion or insertion of specific amino acid positions (site-specific mutagenesis) or non-specific amino acid positions (random mutagenesis) in the beta sheet.

22. Method according to one or more of the preceding claims, characterized in that, the mutants in step b) are expressed in prokaryotic or eukaryotic cells, in a cell-free system as a complex with ribosomes or on the surface of plant or animal cells, yeast cells or phages, viruses or bacteria.

23. Method according to one or more of the preceding claims, characterized in that mutants having the desired binding properties are selected by contacting these mutants with the binding partner and isolating those mutants having the desired binding affinity.

24. Method according to one or more of the preceding claims, characterized in that
mutants having the desired catalytic properties are selected by contacting these mutants with their substrate and isolating those mutants having the desired catalytic activity.

25. Use of a protein according to one or more of the preceding claims in diagnostics and therapy, in cosmetics, bioseparation and biosensors and reduction of harmful substances.